

## CLAIMS

1. A pharmacologically active peptide hormone derivative in which the parent peptide hormone has been modified by 5 introducing either a lipophilic substituent, W, in the N-terminal amino acid or a lipophilic substituent, Z, in the C-terminal amino acid of the parent peptide hormone or an analogue thereof, said lipophilic substituent having from 8 to 10 carbon atoms, with the proviso that when the lipophilic substituent is attached to the N-terminal amino group then the substituent comprises a group which can be negatively charged and with the further proviso, that said peptide hormone is not insulin or an analogue thereof.

15 2. A peptide hormone derivative according to claim 1 wherein a lipophilic group, W, is present.

3. A peptide hormone derivative according to claim 2 wherein W has from 12 to 35 carbon atoms.

20 4. A peptide hormone derivative according to claim 1 wherein a lipophilic group, Z, is present.

5. A peptide hormone derivative according to claim 4 wherein Z 25 has from 12 to 35 carbon atoms.

6. A peptide hormone derivative according to claim 1 wherein the parent peptide hormone is selected from the group consisting of ACTH, corticotropin-releasing factor, 30 angiotensin, calcitonin, glucagon, glucagon-like peptide and analogues and fragments thereof, IGF-1, IGF-2, enterogastrin, somatostatin, somatotropin, somatomedin, parathyroid hormone, thrombopoietin, erythropoietin, hypothalamic releasing factors, prolactin, thyroid stimulating hormones, endorphins, 35 enkephalins, vasopressin, oxytocin, opioids and analogues thereof, superoxide dismutase, interferon, asparaginase, arginase, arginine deaminase, adenosine deaminase and

ribonuclease.

7. A peptide hormone derivative according to claim 2 wherein a carboxyl group contained in W forms an amide bond together with the  $\alpha$ -amino group of the N-terminal amino acid.

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8. A peptide hormone derivative according to claim 2 wherein a carboxyl group contained in W forms an amide bond together with the  $\epsilon$ -amino group of a N-terminal lysine.

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9. A peptide hormone derivative according to claim 2 wherein W is  $\text{CH}_3(\text{CH}_2)_n((\text{CH}_2)_m\text{COOH})\text{CHNH-CO}(\text{CH}_2)_2\text{CO-}$  where n and m are integers and W has from 8 to 40, preferably from 12 to 35 carbon atoms.

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10. A peptide hormone derivative according to claim 2 wherein W is a group of the general formula  $\text{CH}_3(\text{CH}_2)_r\text{CO-NHCH}(\text{COOH})(\text{CH}_2)_2\text{CO-}$  wherein r is an integer from 10 to 24.

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11. A peptide hormone derivative according to claim 2 wherein W is a group of the general formula  $\text{CH}_3(\text{CH}_2)_s\text{CO-NHCH}((\text{CH}_2)_2\text{COOH})\text{CO-}$  wherein s is an integer from 8 to 24.

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12. A peptide hormone derivative according to claim 4 wherein an amino group contained in Z forms an amide bond together with carboxyl group of the C-terminal amino acid.

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13. A peptide hormone derivative according to claim 4 wherein Z is a group of the general formula  $-\text{NHCH}(\text{COOH})(\text{CH}_2)_4\text{NH-CO}(\text{CH}_2)_m\text{CH}_3$  wherein m is an integer from 8 to 18, that is, Z is a N $\epsilon$ -acylated lysine residue.

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14. A peptide hormone derivative according to claim 4 wherein Z is a group of the general formula  $-\text{NHCH}(\text{COOH})(\text{CH}_2)_4\text{NH-COCH}((\text{CH}_2)_2\text{COOH})\text{NH-CO}(\text{CH}_2)_p\text{CH}_3$  wherein p is an integer from 10 to 16.

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15. A peptide hormone derivative according to claim 4 wherein  
Z is a group of the general formula  $-\text{NHCH}(\text{COOH})(\text{CH}_2)_4\text{NH}-$   
 $\text{CO}(\text{CH}_2)_2\text{CH}(\text{COOH})\text{NH}-\text{CO}(\text{CH}_2)_q\text{CH}_3$ , wherein q is an integer from 10  
5 to 16.

16. A peptide hormone derivative according to claim 4 wherein  
Z is a group of the general formula  $-\text{NHCH}(\text{COOH})(\text{CH}_2)_4\text{NH}-$   
 $\text{CO}(\text{CH}_2)_2\text{CH}(\text{COOH})\text{NHCO}(\text{CH}_2)_t\text{CH}_3$ , wherein t is zero or an integer  
10 from 1 to 22.

17. A peptide hormone derivative according to claim 4 wherein  
a spacer in the form of the dipeptide Gly-Lys has been  
inserted between the lipophilic group Z and the parent peptide  
15 hormone.

18. A peptide hormone derivative according to claim 4 wherein  
Z comprises a partly or completely hydrogenated  
cyclopentanophenanthrene skeleton.

20 19. A method of providing a pharmacologically active peptide  
hormone derivative which has a protracted profile of action  
relative to the parent peptide hormone which method comprises  
modifying the parent peptide hormone by introducing either a  
25 lipophilic substituent, W, in the N-terminal amino acid or a  
lipophilic substituent, Z, in the C-terminal amino acid of the  
parent peptide hormone, said lipophilic substituent having  
from 8 to 40 carbon atoms, with the proviso that when the  
lipophilic substituent is attached to the N-terminal amino  
30 group then the substituent comprises a group which can be  
negatively charged and with the further proviso, that said  
peptide hormone is not insulin or an analogue thereof.